

**REMARKS**

Review and reconsideration on the merits are requested.

Prior art considered: U.S. Patent 5,180,750 Sugaya et al (Sugaya); U.S. Patent 4,273,878 Amick (Amick).

The rejections: claims 1-4 and 7-14 are rejected under 35 U.S.C. § 102(b) as anticipated by Sugaya and Amick.

The Examiner's reading of the prior art is set forth in the Action and will not be repeated here except as necessary to an understanding of Applicants' traversal which is now presented.

**Traversal**

Prior to discussing the prior art, Applicants wish to emphasize that in order for an anticipation rejection to be proper every limit of the claims must be set forth in a single prior art reference, either explicitly or implicitly. Applicants respectfully submit that in the present instance, the Examiner provides insufficient basis to support an anticipation rejection, simply stating that Sugaya and Amick teach anion exchange resins for separation using polyamine crosslinkers.

Applicants now turn to the prior art and establish that, in fact, the anticipation rejections are improper.

**Sugaya**

Sugaya discloses an anion exchanger which is used as an anion exchanger membrane such as a hollow fiber-type anion exchange membrane and a porous anion exchange membrane (column 1, lines 4-17). Sugaya is completely silent on an anion exchanger in fine particle form.

The anion exchange membrane of Sugaya consists essentially of an aromatic polysulfone block copolymer having anion exchange groups (column 4, lines 46-48; claim 1). The anion exchange groups are introduced by chloromethylation, followed by amination (claim 2). The amination of chloromethylated polysulfone polymer can be effected by crosslinking with a polyamine (column 8, line 8-column 9, line 27; claim 7). However, quite clearly Sugaya is completely silent on the molecular weight of the Sugaya polyamine. Polyamines are specifically recited in the paragraph at column 9, lines 1-27 of Sugaya and polyethyleneimine is specifically mentioned (column 9, lines 7-8). However, the polyamines specifically recited in Sugaya at this point appear to be low molecular weight compounds, and the number average molecular weight of these compounds would thus be far smaller than 50,000.

In summary, Sugaya is completely silent on an anion exchanger in fine particle form and on the molecular weight of the Sugaya polyamine. Thus, Applicants submit that the instant claims are neither anticipated by nor obvious over Sugaya.

Regarding pore diameter, Sugaya discloses a pore size of from 0.01 to 5  $\mu\text{m}$  (col. 10, lines 41-43). However, the pores are not in fine particles, rather, are in a membrane.

#### **Amick**

Amick discloses an anion exchange resin produced by reacting a stabilized polychlorostyrene polymer bead with a polyamine (Abstract, column 1, line 50 - column 2, line 7, claim 1).

Various types of polyamines are recited by chemical formulae (a) through (k) in the paragraphs at column 3, line 63-column 5, line 46 of Amick. However, these polyamines are

low molecular weight compounds. Applicants have calculated the maximum molecular weights of polyamines in each of chemical formulae (a) through (k). The calculations were based on the largest numerical value of each of suffixes: n, n', n'', m, m', y and z in chemical formulae (a) through (k). Applicants calculated maximum molecular weights of the polyamines are as follows.

(a) 256, (b) 271, (c) 332, (d) 451, (e) 288, (f) 796,  
(g) 580, (h) 504, (i) 692, (j) 754, (k) 804.

Quite clearly these molecular weights are far smaller than the 50,000 recited in claim 1 herein.

To provide an anion exchanger in fine particle form which exhibits a high adsorption capacity for proteins or other objective samples according to the present invention, it is important that a polyamine having a number average molecular weight of at least 50,000 be bound to the surface of the fine particles. The Examiner is requested to compare Example 1 with Comparative Example 1 in the present specification, summarized below.

	Molecular weight of polyethyleneimine	Adsorption capacity for protein (mgBSA/ml.gel)	Chromatogram for protein separation
Example 1	70,000	80	(A) in Fig.1
Comp. Ex. 1	600	42	(B) in Fig.1
ditto	1,800	40	-
ditto	10,000	43	-

As can be seen from the above table, when the molecular weight of a polyethyleneimine is 10,000 or less, the adsorption capacities for protein are small, and there is no great difference among adsorption capacities. In distinction, when the molecular weight of polyethyleneimine is

at least 50,000 (e.g., 70,000), the adsorption capacity for proteins is about twice that of a polyethyleneimine of MW=10,000 or less.

With respect to claim 2 of the present application, Amick mentions beads sizes in the Amick examples (column 8, lines 1 and 46). However, Amick is silent as to whether the beads have pores or not. The Examiner is requested to note, in this regard that the bead size is expressed in terms of “mesh” in Amick. Applicants advise, however, that the meaning of “-20/+100” and “-40/+50” is unclear to them as they could not find these ASTM or Tyler standards.

In Amick, the beads are made by a process where a monovinyl aromatic monomer is polymerized to form linear polymer beads containing chloromethyl groups; such beads are stabilized; and then the stabilized beads are aminated to thereby crosslink and render the beads insoluble in solvents (column 2, line 10 to column 4, line 2). The Inventors herein would like to point out that porous beads are difficult to prepare by this process, and, further that, if the degree of crosslinking with the polyamine is extremely low, the beads are swollen in water and may have pores, but such beads are very soft and have no practical use. See later “Discussion A”.

In summary, Amick teaches crosslinking of linear polymer beads with a low molecular weight polyamine, but contains no teaching about crosslinking with a polyamine having a number average molecular weight of at least 50,000.

Applicants submit that it is surprisingly unexpected from Amick that a far higher adsorption capacity for proteins and other materials, as compared with low molecular weight

polyamines, would be obtained with a polyamine having a number average molecular weight of at least 50,000.

Withdrawal of the anticipation rejection is requested.

New claim 15 is added finding basis at page 6, lines 3-7 of the specification.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

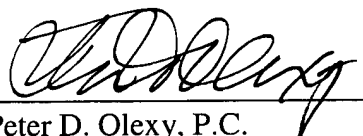
#### Discussion A

There is no particular point in the specification of the present application suggesting that the beads of Amick are not porous. Amick teaches that the beads are prepared by a process where linear polymer beads are prepared by suspension polymerization; the linear polymer beads are stabilized, and then subjected to swelling in an organic solvent; and then, the swollen beads are crosslinked with polyamine (col. 2, line 10 (including flow diagram) to col. 3, line 22). Amick does not disclose any procedure for producing porous polymer beads. Porous polymers can be prepared, for example, by copolymerization of a polyfunctional monomer (i.e., crosslinking monomer), or by incorporation of a blowing agent into a polymer followed by heating. Pores are not formed when swollen polymer beads are crosslinked with polyamine in the preparation process taught in Amick. A preferred fine polymer particle used in the present invention is prepared by copolymerization of a polyfunctional monomer as suggested on page 6, lines 8-34.

AMENDMENT UNDER 37 C.F.R. § 1.111  
U.S. Application No.: 10/051,195

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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